UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY
CAMDEN VICINAGE

IN RE: VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION	MDL No. 2875 Honorable Robert B. Kugler, District Court Judge **Oral Argument Requested**

MEMORANDUM OF LAW IN SUPPORT OF DEFENDANTS' MOTION TO PARTIALLY EXCLUDE OPINIONS OF DRS. STEPHEN HECHT AND RAMIN NAJAFI

TABLE OF CONTENTS

Page

TABLE OF AUTHORITIES

Page(s)

CASES

INTRODUCTION

Drs. Stephen Hecht and Ramin ("Ron") Najafi seek to parlay their expertise as chemists into improper advocacy on a wide range of topics. While these experts are qualified to testify about the chemical processes used by Zhejiang Huahai Pharmaceutical Co., Ltd. ("ZHP") to manufacture its valsartan active pharmaceutical ingredient ("API"), many of their opinions lack a reliable scientific basis, were not properly disclosed, fall far outside their expertise, and/or are not proper subjects for expert testimony. Those opinions should be excluded.

First, the fundamental premise of Drs. Hecht and Najafi's opinions is that reasonable chemists should have known that the "Zinc Chloride" and "TEA with quenching" processes for valsartan API were capable of forming two nitrosamines, NDMA and NDEA, at the time those processes were being developed and used.[1] But neither Dr. Hecht nor Dr. Najafi has identified ***any*** scientific literature or evidence reporting the formation of either NDMA or NDEA – or even the chemicals required to form those impurities – in the conditions in which valsartan API was manufactured. Further, Dr. Najafi, who has a Ph.D. in chemistry and runs a testing laboratory, expressly admitted that he did not know it was possible for the reaction

[1] Amines are compounds made up of nitrogen and one or more alkyl groups. Nitrosamines are organic molecules with a nitroso group bonded to a deprotonated amine, i.e., an amine that has lost an H+ ion. A secondary amine includes two alkyl groups (and one hydrogen atom), and it is by far the most likely amine to form a nitrosamine.

used by ZHP in the TEA with quenching process to result in the formation of NDEA prior to being retained in this litigation.[2]

Second, to the extent Drs. Hecht and Najafi tried to pivot at their depositions to a new theory that ZHP should have known that certain raw materials purchased by ZHP could be contaminated with substances capable of reacting to form NDEA and/or NDMA, such opinions are inadmissible because they were not properly disclosed in the experts' reports and do not "fit" the facts of this case.

Third, Drs. Hecht and Najafi should also be barred from opining that ZHP (or any other defendant) failed to comply with regulatory requirements because they

[2] At his deposition, Dr. Hecht repeatedly confirmed that he was not offering opinions or criticisms of Teva's or Torrent's failure to detect the impurities, their risk assessment of ZHP API, or their testing of ZHP's API. (*See, e.g.*, Dep. of Stephen Hecht, Ph.D. ("Hecht Dep.") 251:8-23, Jan. 13, 2023 (Ex. 1 to the Certification of Jessica Davidson ("Davidson Cert.")) ("Q. In this [October 2022] report, are you intending to offer any opinions with regard to the finished-dose manufacturers? . . . A. No."); 252:16-254:12 (discussing portions of his "July 6, 2021" report and indicating that the identified portions of the report were not a criticism of Teva's conduct); 255:15-18 (Dr. Hecht testifying that he did not mention "either of the finished-dose manufacturers" in the first two paragraphs of his October 2022 report summarizing his opinions); 255:19-256:11 (Dr. Hecht confirming references to Teva and Torrent were not opinions or criticisms of Teva or Torrent); 265:6-12 (confirming he had not "looked at" the issue of "whether the finished-dose manufacturers, including Teva, should have recognized the potential for nitrosamine formation, based on the information that was available to them about ZHP's process at the time they submitted their ANDAs"); 286:21-288:7 (Dr. Hecht confirming portions of his July 2021 report did not offer opinions or criticisms of Torrent). Teva and Torrent nonetheless join this motion with respect to Dr. Hecht in an abundance of caution.

lack regulatory qualifications and such testimony would constitute improper legal opinions. Indeed, this Court has already partially excluded Dr. Najafi's opinions on this ground.

Finally, Dr. Najafi should be barred from testifying that valsartan poses an "unreasonable safety risk to patients" because he is not a medical doctor, toxicologist or epidemiologist and therefore lacks the qualifications to opine on general causation.

BACKGROUND

Plaintiffs have submitted expert reports from two chemists in support of their claims that ZHP violated Current Good Manufacturing Practices ("cGMPs") in manufacturing API: Dr. Najafi and Dr. Hecht.

Dr. Najafi, a chemist, has never "worked at [the] FDA," or "done any consulting work for the FDA" and has never "worked in regulatory affairs for any generic [drug] manufacturer[]." (Dep. of Ramin ("Ron") Najafi, Ph.D. ("1/18/23 Najafi Dep.") 19:13-18, Jan. 18, 2023 (Ex. 2 to Davidson Cert.); Dep. of Ramin ("Ron") Najafi, Ph.D. ("2/3/22 Najafi Dep.") 156:12-18, Feb. 3, 2022 ("2/3/22 Najafi Dep.") (Ex. 3 to Davidson Cert.).) Dr. Najafi also is "not a medical doctor, toxicologist, or epidemiologist." (1/18/23 Najafi Dep. 67:17-19.) Accordingly, he agreed that he was not seeking to offer any opinions about "whether nitrosamines are genotoxic or can cause cancer," "the toxicity of nitrosamines," "the level of

exposure to nitrosamines . . . capable of causing cancer," or whether "a specific patient developed cancer as a result of taking valsartan." (*Id.* 67:2-16.)

Like Dr. Najafi, Dr. Hecht is a chemist who is not "an expert in regulatory or FDA issues," and has no experience with pharmaceutical regulation and enforcement. (Hecht Dep. 35:12-16, 239:3-10.)

In their reports, Drs. Najafi and Hecht both generally assert that: (1) NDEA was formed as a result of various reactions during ZHP's TEA with quenching manufacturing process; and (2) NDMA was formed as a result of various reactions during the Zinc Chloride process. (Report of Ramin "Ron" Najafi, Ph.D. ("10/31/22 Najafi Rep.") at 27-28, Oct. 31, 2022 (Ex. 4 to Davidson Cert.); Report of Stephen Hecht, Ph.D. ("7/6/21 Hecht Rep.") at 21-22, July 6, 2021 (Ex. 5 to Davidson Cert.).) Defendants do not seek to exclude that testimony. However, both experts also seek to opine that ZHP conducted insufficient risk analyses and testing in connection with developing and using the new manufacturing processes because it should have known that the reactions involved could result in the formation of NDEA or NDMA – and therefore should have specifically looked for those nitrosamines in the resulting API. (10/31/22 Najafi Rep. at 27; Report of Stephen Hecht, Ph.D. ("10/31/22 Hecht Rep.") at 4, Oct. 31, 2022 (Ex. 6 to Davidson Cert.).) Following is a summary of the experts' opinions and testimony on those issues:

NDEA. Prior to April 2012, ZHP manufactured its valsartan API using a process that involved both triethylamine ("TEA") and sodium azide. (10/31/22 Najafi Rep. at 19.) When that process is complete, the sodium azide must be removed from the final API for patient safety, and in April 2012, ZHP added a "quenching procedure . . . to guarantee [the sodium] azide is destroyed thoroughly and to minimize the risk of residual [sodium] azide carry-over into the final drug substance." (*Id*.) According to both Drs. Hecht and Najafi, this new manufacturing process – known as TEA with quenching – resulted in the formation of NDEA. Dr. Najafi's primary theory is that the TEA degraded into diethylamine ("DEA"), a secondary amine, and that the secondary amine, in turn, reacted with a nitrosonium ion ($NO+$)[3] derived from the sodium nitrite ($NaNO_2$) used in the quenching step to create NDEA. (*See* 10/31/22 Najafi Rep. at 24.) This final reaction is referred to as nitrosation, because it results in a nitrosamine.

Dr. Hecht took the position in his general causation report that the nitrosation occurred directly from the tertiary amine TEA, without any prior degradation to a secondary amine. (*See* 7/6/21 Hecht Rep. at 21.) And, in his liability report, Dr. Hecht states that the quenching process used during the manufacture of valsartan API "led to a reaction between foreseeably created ***secondary amines*** and the nitrous

[3] A nitrogen atom bonded to an oxygen atom with one electron removed.

acid to create NDMA/NDEA." (10/31/22 Hecht Rep. at 1 (emphasis added).) But nitrosation of a tertiary amine like TEA is extremely rare (*see* 7/6/21 Hecht Rep. at 18; Report of Fengtian Xue at 17-18, Dec. 22, 2022 (relevant excerpts attached as Ex. 7 to Davidson Cert.)), and Dr. Hecht did not cite any scientific literature in either his current or prior reports in this litigation that documents such a reaction between TEA and sodium nitrite prior to or during the time that the TEA with quenching process was being used to manufacture ZHP's API (i.e., from April 2012 to June 2018). (*See generally* 10/31/22 Hecht Rep.; 7/6/21 Hecht Rep.) Indeed, Hecht's general causation report merely states that "[t]ertiary amines can also be nitrosated to form dialkylnitrosamines such as ***NDMA***," with no reference to NDEA. (7/6/21 Hecht Rep. at 6 n.4 (emphasis added).) Further, the one article Dr. Hecht cites for this proposition addressed the potential nitrosation of two ***different*** tertiary amines, tribenzylamine and N-N,dibenzylaniline, not TEA. Peter Smith & Richard Loeppky, *Nitrosative Cleavage of Tertiary Amines*, J. Am. Chem. Soc. 89, 1147-1157, at 1147 (1967) ("Smith (1967)") (Ex. 8 to Davidson Cert.). And that article undermines the notion that those reactions were well known insofar as it discusses "the assumed inertness of tertiary amines" and states that "[s]carcely a textbook currently in print suggest[ed]" they could nitrosate. *Id.* at 1147-48.

In his report, Dr. Najafi cited a single webpage addressing the laboratory uses of sodium azide to support his assertion that it is a "well-established textbook

reaction" that TEA in the presence of sodium nitrite can be nitrosated to form NDEA. (*See* 10/31/22 Najafi Rep. at 27-28 (citing https://chem.libretexts.org/Ancillary_Materials/Demos_Techniques_and_Experiments/Chemical_Safety/Reagent_Specific_Hazards/Sodium_Azide (Ex. 9 to Davidson Cert.)).) But that webpage does not mention TEA, sodium nitrite, or NDEA, and Dr. Najafi admitted at his deposition that it was "incorrectly cited." (1/18/23 Najafi Dep. 182:6-20.)

After a break in the deposition, plaintiffs' counsel provided defendants with a new, previously undisclosed article that Dr. Najafi ultimately claimed was the "only article" he reviewed prior to forming his opinion that nitrosamines could form from tertiary amines such as TEA.[4] (*See id*. 223:19-225:1; 1/24/23 Najafi Dep. 283:19-25.) In that article – RN Loeppky et al, *Ester-mediated nitrosamine formation from nitrite and secondary or tertiary amines*. IARC Sci Publ. 1984; (57):353-63 ("Loeppky (1984)") (Ex. 11 to Davidson Cert.) – the authors observed that certain *N*-nitrosamines were formed when various secondary and tertiary amines were heated with sodium nitrite in the presence of diacetyl glycol (also called ethylene

[4] Plaintiffs' counsel also provided defendants with an additional article on which Dr. Najafi purportedly relied for the proposition that it was "textbook" science that TEA could react with sodium nitrite to form NDEA. But on the second day of his deposition, Dr. Najafi testified that he had not read that other article in full and was "not relying on th[at] article for [his] opinion." (Dep. of Ramin ("Ron") Najafi, Ph.D. 282:12-21, 283:19-25, Jan. 24, 2023 ("1/24/23 Najafi Dep.") (Ex. 10 to Davidson Cert.).)

glycol diacetate) in an ethylene glycol solution. Loeppky (1984) at 353. But neither ester diacetyl glycol nor ethylene glycol was used by ZHP in the TEA process for manufacturing valsartan, as Dr. Najafi conceded at his deposition. (1/24/23 Najafi Dep. 285:14-17, 287:20-25.)

Dr. Najafi also testified that, despite having a Ph.D. in chemistry and operating his own laboratory, he first became aware of the possibility that TEA exposed to sodium nitrite could ultimately form NDEA in connection with this litigation. (1/18/23 Najafi Dep. 192:18-193:7; *see also id*. 193:8-15 (Dr. Najafi answering "yes" when asked if he learned of the reaction by which TEA could form NDEA "through [his] investigation in connection with this litigation").)

At his deposition, Dr. Najafi advanced the alternative theory that it was also "possible" that the raw TEA used by ZHP in the manufacturing process was contaminated with DEA. (*See* 1/18/23 Najafi Dep. 193:22-24 ("it's very possible that triethylamine has some diethylamine as well").) But this theory is not addressed in Dr. Najafi's report, which claims that NDEA was formed as a result of a series of reactions between ***TEA*** and sodium nitrite. (10/31/22 Najafi Rep. at 24.) And while Dr. Hecht's report quotes a ZHP document stating that there may have been "diethylamine impurities in triethylamine hydrochloride" (10/31/22 Hecht Rep. at 10), that document merely summarizes a theory ***proposed by ZHP*** in investigating the potential root cause of the NDEA in valsartan ***after*** it was discovered. (*See*

PRINSTON00075797 at -5977 (relevant excerpts attached as Ex. 12 to Davidson Cert.).)

NDMA. In December 2013, ZHP introduced a new manufacturing process known as the Zinc Chloride process. (10/31/22 Najafi Rep. at 24.) The Zinc Chloride process "changed the chemical reagent . . . from [TEA] to zinc chloride" and added the solvent dimethylformamide ("DMF") to "facilitate the process." (*Id*.)

Both Drs. Najafi and Hecht opine in their reports that this change led to the formation of NDMA because the DMF solvent degraded into a secondary amine called dimethylamine ("DMA"), which was then nitrosated by a nitrosonium ion (NO+) derived from the sodium nitrite ($NaNO_2$) in the quenching process to create NDMA. (*See* 10/31/22 Najafi Rep. at 26; 7/6/21 Hecht Rep. at 18, 20; 10/31/22 Hecht Rep. at 5, 7.) Dr. Najafi seeks to offer the opinion that ZHP's use of the "DMF solvent in the [Zinc Chloride] process should have raised concern for the possible formation of nitrosamines because DMF solvent has been long known to decompose into [DMA]." (10/31/22 Najafi Rep. at 26.) Dr. Hecht similarly claims that DMF was "well known to decompose/degrade forming" DMA. (7/6/21 Hecht Rep. at 18.) But Dr. Najafi cites only one publication in his report, an Australian textbook, that purportedly documents the degradation of DMF into DMA. (*See* 10/31/22 Najafi Rep. at 26 (citing *Purification of Laboratory Chemicals*, Armarego, WLF (4th Edition 1996; 6th Edition 2009) ("Armarego") (relevant excerpts attached as Ex. 13

to Davidson Cert.)).) And Dr. Hecht cites only the Armarego textbook and a 2009 article that references it. (*See* 7/6/21 Hecht Rep. at 18 n.85 (citing J. Muzart, *N,N-Dimentylformamide: much more than a solvent*, Tetrahedron 65, 8313-8323 ("Muzart (2009)") (Ex. 14 to Davidson Cert.)).)

The Armarego textbook is more than 500 pages long and includes only two sentences regarding the decomposition of DMF, stating that DMF:

> Decomposes ***slightly at its normal boiling point*** to give small amounts of dimethylamine and carbon monoxide. The decomposition is catalysed by acidic or basic materials, so that even at room temperature DMF is appreciably decomposed if allowed to stand for several hours with solid KOH, NaOH or CaH2.

Armarego at 192 (emphasis added). The textbook also states that the boiling point of DMF at sea level is 153° Celsius. The highest temperature reached in ZHP's Zinc Chloride process was significantly lower than the boiling point of DMF, as both Drs. Najafi and Hecht admitted at their depositions. (1/18/23 Najafi Dep. 206:11-19 ("**Q.** Do you know the highest temperature that occurred during the Step 4 of the zinc chloride process? . . . [**A.**] I think it was probably around hundred degrees . . . . **Q.** So lower than the boiling point of DMF. Correct? **A.** Correct."); Hecht Dep. 218:7-15 (Dr. Hecht stating that the Zinc Chloride process was run at "18 degrees [Celsius] lower" than the boiling point of DMF).) Nothing in Armarego suggests that DMF could degrade at that temperature.

Drs. Hecht and Najafi have not offered any evidence that the passage in Armarego was widely publicized within the field of chemistry such that any reasonable chemist should have been aware of it. Indeed, Dr. Najafi testified that he only became aware of the Armarego textbook after he was retained as an expert in this litigation. (1/18/23 Najafi Dep. 203:2-4.) And Dr. Hecht testified that he does not know whether the statements in Armarego about the ability of DMF to degrade into DMA are widely known even today. (*See* Hecht Dep. 211:8-11, 212:5-12.) In addition, Dr. Najafi admitted that he has "used DMF, you know, many, many, many times, and I have not, you know, made an observation that it causes degradation into dimethylamine." (1/18/23 Najafi Dep. 109:2-9.)

In the alternative, Drs. Najafi and Hecht suggested that the raw DMF used by ZHP in the Zinc Chloride process was contaminated with dimethylamine when purchased. (*See* 1/18/23 Najafi Dep. 198:13-199:2; Hecht Dep. 46:1-9.) But neither expert's report identifies any scientific literature stating that DMF is contaminated with DMA, much less demonstrating that this possibility was well known by chemists at the time the valsartan at issue was being manufactured. And there is no evidence in the record that the DMF purchased by ZHP for use in the Zinc Chloride process contained even trace amounts of DMA as a contaminant. Indeed, Dr. Hecht acknowledged that the only testing of the DMF used by ZHP that he reviewed ***found no DMA***. (*See* Hecht Dep. 66:9-13 ("**Q.** Do you remember what was concluded

from that analysis you're referring to? **A.** Yes, I believe they checked the sample of DMF and -- for dimethylamine, and they didn't find any.").)

ARGUMENT

The standards governing the admissibility of expert testimony are set forth in Defendants' Memorandum of Law in Support of Motion to Exclude Opinions of Dr. Laura M. Plunkett, and incorporated fully herein.

A number of the opinions offered by Drs. Hecht and Najafi are inadmissible under these standards.

I. DRS. HECHT AND NAJAFI LACK A RELIABLE BASIS TO OPINE THAT ZHP OR ANY DEFENDANT SHOULD HAVE KNOWN THAT ZHP'S MANUFACTURING PROCESSES WOULD RESULT IN THE FORMATION OF NDMA OR NDEA.

The Court should bar Drs. Hecht and Najafi from testifying at trial that any reasonable chemist would have known about the potential for the formation of NDMA and NDEA during the valsartan manufacturing process because the experts have no scientific or otherwise objective basis for those opinions. *See In re 3M Combat Arms Earplug Prods. Liab. Litig.*, No. 3:19md2885, 2021 WL 684183, at *4 (N.D. Fla. Feb. 11, 2021) (barring audiologist from opining "on what was 'understood' or 'well-known' by 'the military' or 'the military audiology community' regarding hearing protection in general or the [hearing protection device at issue] more specifically" absent objective evidence "such as a survey or a widely distributed publication"); *Grimes v. Hoffmann-LaRoche, Inc.*, 907 F. Supp. 33, 37-

38 (D.N.H. 1995) (excluding opinion about a supposedly "generally accepted scientific fact" because the expert's view on what was accepted was an "untested assumption").[5] Nor should they be allowed to offer opinions that are premised on these inadmissible opinions – i.e., that ZHP, Teva or Torrent should have conducted a different risk assessment prior to or as a result of ZHP's manufacturing changes.

A. TEA And NDEA Formation.

As noted above, despite his claim that nitrosation of TEA into NDEA is a "well-established textbook reaction" that the chemists at ZHP should have anticipated (Najafi 10/31/22 Rep. at 27-28), Dr. Najafi did not identify ***any*** textbook or other scientific literature to this effect in his report and admitted at his deposition that the one webpage he cited was "an incorrect citation" (1/18/23 Najafi Dep. 182:18-20). Moreover, the article Dr. Najafi identified at his deposition, Loeppky (1984), comes nowhere close to establishing that it is "textbook" knowledge that TEA will react with sodium nitrite to form NDEA, much less that it could have

[5] *See also Lea v. Wyeth LLC*, No. 1:03-CV-001339, 2011 WL 13143427, at *1, *4 (E.D. Tex. Oct. 6, 2011) (excluding expert opinions "regarding the knowledge that [d]efendant[]" pharmaceutical manufacturers "should have had or the actions that [d]efendants should have taken" because they were based on the experts' "personal views" and "lacked a reliable underlying methodology"); *Rebotix Repair, LLC v. Intuitive Surgical, Inc.*, No. 8:20-CV-2274-VMC-TGW, 2022 WL 3226769, at *4 (M.D. Fla. Aug. 10, 2022) (rejecting expert opinion that certain information "'would be' concerning to other surgeons" because the expert failed to use "any method to learn of the perceptions of these other groups, outside of his own speculation").

occurred in the TEA with quenching process. Rather, the focus of that article was on the "the unusual role" played by ethylene glycol, which was used as a solvent in the authors' experiments, as well as the diester diacetyl glycol (ethylene glycol diacetate). Loeppky (1984) at 353-54. As Dr. Najafi admits, the TEA with quenching process did not use either chemical. (*See* 1/24/23 Najafi Dep. 285:14-17, 288:11-13.) And even if it had, it would be absurd to suggest that one article in one journal was so widely read that it would have put all reasonable chemists on notice that TEA could become nitrosated, forming NDEA. Indeed, as noted above, Dr. Najafi did not know about this possibility until after he was retained in the litigation and began to research nitrosamine issues to prepare his expert report. (*Id*. 294:4-10.)

Dr. Hecht similarly has not identified any literature supporting his opinion that the TEA with quenching process "foreseeably created secondary amines" that reacted with "the nitrous acid to create . . . NDEA." (*See* 10/31/22 Hecht Rep. at 1.) Dr. Hecht cited one article in his general causation report for the proposition that "[t]ertiary amines can also be nitrosated to form dialkylnitrosamines such as ***NDMA***," but that article did not address either TEA or NDEA. (7/6/21 Hecht Rep. at 6 (emphasis added).) Rather, that article discussed two other tertiary amines, Smith (1967) at 1148, and in doing so, noted that the question of whether tertiary

amines could ever be nitrosated was controversial because it had been generally "assumed" that tertiary amines were "inert[]," *id.* at 1147-57.

In short, Drs. Hecht and Najafi have not identified any scientific literature to support the assertion that it was well known among chemists prior to 2018 that the reactions in ZHP's TEA with quenching process could lead to the formation of NDEA. Accordingly, these opinions and all of their corollaries, including the two experts' opinions related to any defendant's risk assessment procedures, should be excluded from trial.

B. Zinc Chloride Process And NDMA Formation.

Drs. Hecht and Najafi both seek to opine that ZHP should have expected the production of NDMA in the Zinc Chloride process because it has long been known that DMF can degrade into dimethylamine (which can then form NDMA). (*See, e.g.*, 10/31/22 Najafi Rep. at 26 ("DMF solvent has been long known to decompose into dimethylamine."); 7/6/21 Hecht Rep. at 18 (asserting that DMF "was well known to decompose/degrade forming dimethylamine").) These opinions are not reliable either.

As explained above, Drs. Hecht and Najafi place enormous weight on one sentence in an Australian textbook entitled *Purification of Laboratory Chemicals* by

Armarego,[6] in which the author states that DMF "[d]ecomposes slightly at its normal boiling point to give small amounts of dimethylamine and carbon monoxide." Armarego at 192. But the reaction that forms valsartan did not come close to the boiling point, as the experts admitted in their depositions.[7] (1/18/23 Najafi Dep. 206:11-19; Hecht Dep. 218:4-15.) Instead, Drs. Hecht and Najafi testified that it was "basic chemistry" that a substance like DMF would degrade at temperatures lower than its boiling point. (*See, e.g.*, Hecht Dep. 94:9-13 ("I mean, there's no doubt that DMF can hydrolyze to dimethylamine when you heat it for 20 hours at 135 degrees, or whatever it was. I mean, that's like basic organic chemist -- chemistry."); 1/18/23 Najafi Dep. 208:17-19 ("That, you know, if it degrades at 153, it will gradually degrade, very gradually degrade at 30 degrees, 40 degrees Celsius.").) This is pure *ipse dixit*; neither Dr. Hecht nor Dr. Najafi has provided any scientific support for that claim.

In any event, even if the Armarego textbook had addressed DMF degradation under circumstances analogous to the manufacture of valsartan, that would still not

---

[6] As noted above, Dr. Hecht also cites Muzart (2009) for this proposition, but that article merely references and repeats the statements about DMF degradation contained in Armarego. (*See* 7/6/21 Hecht Rep. at 18 n.85.)

[7] The textbook also states that "even at room temperature DMF is appreciably decomposed if allowed to stand for several hours with solid KOH, NaOH or CaH_2." Armarego at 192. But neither expert claims that these compounds were present in the manufacturing process or otherwise relies on this statement.

mean that the potential for degradation was widely known in the scientific community. Dr. Hecht testified that he "do[es not] know whether [the information contained in Armarego about the degradation of DMF is] widely known or not." (*See* Hecht Dep. 211:8-11, 212:5-12.) And Dr. Najafi admitted that he had never seen the Australian textbook before he became involved in this litigation (1/18/23 Najafi Dep 202:10-203:9), does not know if any graduate or undergraduate level chemistry programs use the Armarego publication (*id*. 204:10-13), and has never cited it in any of his published work outside litigation (*id*. 204:14-16). Similarly, while Dr. Hecht claimed to be aware of the Armarego publication, he admitted that the book's authors intended to include information that would not be expected to be familiar to scientists (Hecht Dep. 208:15-209:22), he does not know if anyone teaching chemistry courses uses the Armarego publication (*id.* 213:14-214:1), and he has never cited it in any of his published work outside litigation (*id.* 212:15-213:3).

For all of these reasons, both Dr. Hecht and Dr. Najafi lack an objective, scientific basis for their opinion that ZHP or any other defendant should have known that the Zinc Chloride process could result in NDMA formation.[8]

[8] Because neither Dr. Hecht nor Dr. Najafi should be permitted to testify that chemists would have been aware that ZHP's manufacturing processes could lead to NDMA or NDEA formation, they likewise cannot offer their derivative opinions about the purported inadequacy of ZHP's (or any other defendant's) risk *(cont'd)*

II. DRS. HECHT AND NAJAFI SHOULD BE BARRED FROM TESTIFYING ABOUT THE POSSIBILITY OF CONTAMINATION IN RAW MATERIALS USED BY ZHP.

At their depositions, Drs. Najafi and Hecht sought to offer new opinions to the effect that diethylamine and dimethylamine were known contaminants in certain raw materials used by ZHP – and that ZHP should have been aware of the potential for NDMA or NDEA for that reason as well. (*See, e.g.*, 1/18/23 Najafi Dep. 193:21-24, 198:13-199:2; Hecht Dep. 46:1-9.) These opinions should be rejected for two reasons.

First, they were not properly disclosed in the experts' reports. "[I]t is axiomatic that an expert may not present new opinions on topics not timely included or otherwise disclosed in the expert's report." *See Krys v. Aaron*, 112 F. Supp. 3d 181, 207 (D.N.J. 2015). Dr. Najafi's report does not include ***any*** statement or opinion that the TEA used by ZHP in the TEA with quenching process could have been contaminated with diethylamine. And while Dr. Hecht's general causation and liability reports each include a single mention of "trace amounts of [DEA] present

assessments. (10/31/22 Najafi Rep. at 27 (risk assessment required because possibility of nitrosamine formation was "well-established").) *See, e.g.*, *In re Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, 858 F.3d 787, 797 (3d Cir. 2017) (noting that any unreliable step renders testimony inadmissible); *Coffey v. Dowley Mfg., Inc.*, 187 F. Supp. 2d 958, 976 (M.D. Tenn. 2002) ("[O]nce those foundations are disproved, the whole analysis collapses.").

in the [TEA]"[9] (7/6/21 Hecht Rep. at 21; *see also* 10/31/22 Hecht Rep. at 10 (referencing DEA "impurities in [TEA] hydrochloride")), he does not cite any scientific literature supporting the assertion that DEA is a contaminant of TEA, much less that this is a well-known scientific fact of which ZHP should have been aware.[10] Thus, even if the opinion had been properly disclosed, it is mere *ipse dixit* and would still be inadmissible. *See Bowers v. Nat'l Collegiate Athletic Ass'n*, 564 F. Supp. 2d 322, 350 (D.N.J. 2008) (excluding expert opinion that was "based on little more than 'subjective belief or unsupported speculation'") (citation omitted).

Drs. Hecht and Najafi similarly failed to adequately disclose or support the opinion that dimethylamine was a known contaminant of the DMF used in the Zinc Chloride process. Dr. Najafi's 39-page report contains one sentence stating that "DMF solvent often contains" dimethylamine, without any additional explanation or support. (10/31/22 Najafi Rep. at 26.) And while Dr. Hecht stated in his general causation report that "the contamination of [DMF] with [DMA] . . . was foreseeable,

---

[9] This paragraph of Dr. Hecht's report refers twice to "trimethylamine" as being contaminated with diethylamine and degrading into NDEA. Trimethylamine was never used in the TEA with quenching process (or any other valsartan process), and in any event, it would degrade into NDMA, not NDEA. Defendants assume these to be typographical errors for triethylamine, commonly called TEA.

[10] Dr. Hecht's reference to "diethylamine impurities in triethylamine" in his most recent report is not an opinion but a quote from ZHP's ***post-recall*** Deviation Investigation Report, in which the company proposed initial hypotheses as to how diethylamine became involved in the TEA with quenching process. (10/31/22 Hecht Rep. at 10 (quoting PRINSTON00075797 at -5977).)

and should have been evaluated" (7/6/21 Hecht Rep. at 20), he did not cite any scientific literature to this effect, much less identify evidence capable of establishing that the possibility of DMF contamination was so well known at the time the Zinc Chloride process was being used that ZHP should have tested for it. In addition, the only reference to DMF contamination in Dr. Hecht's 2022 report is a quote from the testimony of ZHP employee Jun Du, who noted that an August 2018 letter from ZHP to the FDA mentioned "the trace amount of [DMA], an impurity/degradant of DMF that reacts with nitrous acid to form NDMA." (10/31/22 Hecht Rep. at 3.) But ZHP's passing reference to dimethylamine as an "impurity/degradant" in its after-the-fact evaluation of the possible sources of dimethylamine in the Zinc Chloride process cannot possibly establish that it was well known in the chemistry community in 2013 that DMF was inherently contaminated with dimethylamine.[11] *See, e.g.*, *Ruggiero v. Yamaha Motor Corp. U.S.A.*, No. 15-49 (JBS/KMW), 2017 WL 1197755, at *8 n.15 (D.N.J. Mar. 31, 2017) ("warning that post-dates the purchases

[11] At his deposition, Dr. Hecht asserted for the first time that the World Health Organization stated in 1994 that DMF sold commercially contained trace amounts of DMA, even though this publication was not cited in his report or reliance list. (Hecht Dep. 59:16-60:12.) As a result, defendants were not afforded sufficient opportunity to test the basis of Dr. Hecht's purported reliance on it. *See, e.g., Liqwd, Inc. v. L'Oreal USA, Inc.*, No. 17-14-JBF-SRF, 2019 WL 10252611, at *1 (D. Del. June 25, 2019) (court must "limit the expert testimony . . . to that disclosed in the expert reports") (citation omitted).

of the [product] at issue here cannot be relied upon to demonstrate what [defendant] knew or should have known the year prior") (citation omitted).

Second, the new contamination opinions offered by Drs. Hecht and Najafi are also inadmissible because there is no evidence of actual contamination in ZHP's raw materials – and these opinions therefore do not "fit" the facts of the case. *See Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579, 591-92 (1993) (explaining that the "'helpfulness' standard requires a valid scientific connection to the pertinent injury as a precondition to admissibility"); *Buzzerd v. Flagship Carwash of Port St. Lucie, Inc.*, 397 F. App'x 797, 800 (3d Cir. 2010) (opinion that did "not fit the central question at issue in the case" properly excluded); *Soldo v. Sandoz Pharms. Corp.*, 244 F. Supp. 2d 434, 564 (W.D. Pa. 2003) (evidence related to different type of stroke was inadmissible because it did "not fit the facts of th[e] case"). Neither Dr. Hecht nor Dr. Najafi claims to have tested the DMF or TEA used by ZHP to determine whether they contained even trace amounts of impurities. Indeed, Dr. Najafi expressly testified that he was ***not*** asked to test DMF. (1/18/23 Najafi Dep. 176:17-177:2.) Nor has either expert identified any other evidence that the DMF or TEA used by ZHP was contaminated. And the existing evidence is to the contrary. In their reports, both Drs. Hecht and Najafi rely on a November 5, 2018 Deviation Investigation Report prepared by ZHP following the valsartan recall, which documents testing performed by ZHP on its raw DMF solvent. (*See* 10/31/22 Najafi

Rep. at 6; 10/31/22 Hecht Rep. at 8 (citing PRINSTON00075797).) But in that testing, DMA ***was not*** detected in the DMF (PRINSTON00075797 at -5948), as Dr. Hecht conceded at his deposition (Hecht Dep. 66:9-13). For this reason, too, the experts' contamination opinions should be excluded.

III. DRS. HECHT AND NAJAFI SHOULD BE PROHIBITED FROM OFFERING REGULATORY OPINIONS.

Drs. Hecht and Najafi should also be barred from testifying about any defendant's compliance with regulatory standards or requirements because: (1) they lack the requisite qualifications to do so; and (2) such opinions are barred under Third Circuit law and this Court's prior rulings.

First, Drs. Najafi and Hecht are not qualified to offer opinions on whether defendants' manufacturing practices or processes adhered to state and federal regulations, because neither possesses any regulatory experience. *See, e.g.*, *Rheinfrank v. Abbott Lab'ys, Inc.*, 680 F. App'x 369, 376, 381 (6th Cir. 2017) (affirming ruling precluding expert with no FDA experience from opining on compliance with FDA requirements); *see also In re Gadolinium-Based Contrast Agents Prods. Liab. Litig.*, No. 1:08 GD 50000, 2010 WL 1796334, at *19 (N.D. Ohio May 4, 2010) (doctor who had studied drug at issue was "not a regulatory expert who has the expertise to opine on FDA regulations and the regulatory process, or whether [defendant] complied with those regulations or process"), *modified on other grounds on reconsideration*, 2010 WL 5173568 (N.D. Ohio June 18, 2010),

aff'd sub nom. Decker v. GE Healthcare Inc., 770 F.3d 378 (6th Cir. 2014); *In re Diet Drugs (Phentermine, Fenfluramine, Dexfenfluramine) Prods. Liab. Litig.*, MDL No. 1203, 2000 WL 876900, at *11 (E.D. Pa. June 20, 2000) (doctors were not qualified "to speak as experts in the field of the requirements of the federal regulations regarding labeling").

Dr. Najafi has taken the position that he is qualified to opine on compliance with cGMP and whether ZHP's API was adulterated because his work as a chemist in a testing lab required him to "become familiar with the regulatory requirements of the FDA." (10/31/22 Najafi Rep. at 2.) But ancillary exposure to regulatory issues while working in the field of chemistry does not render an expert qualified to opine on FDA compliance or regulations. *Rheinfrank*, 680 F. App'x at 376, 381 (affirming exclusion of regulatory testimony by neurologist, geneticist, and epidemiologist). And Dr. Hecht expressly admitted that he is "not really an expert in regulatory or FDA issues." (Hecht Dep. 35:12-16.) For this reason alone, their regulatory opinions should be excluded.

Second, although experts "may sometimes testify on the specific issue of how a government agency applies and enforces its regulations in the context of a complex regulatory regime," *Moorestown Twp. Bd. of Educ. v. S.D.*, No. 10-0312 (RMB), 2010 WL 4062182, at *5 (D.N.J. Oct. 15, 2010), they may not offer their own opinions on a pharmaceutical company's compliance with applicable regulations,

see, e.g., *Stanley v. Novartis Pharms. Corp.*, No. 11-03191 JGB (OPx), 2014 WL 12573393, at *4 (C.D. Cal. May 6, 2014) (precluding an expert from "offer[ing] legal conclusions, including whether [d]efendant was in regulatory compliance with the FDA"); *see also In re Tylenol (Acetaminophen) Mktg., Sales Pracs., & Prods. Liab. Litig.*, MDL No. 2436, 2016 WL 4039324, at *4 (E.D. Pa. July 27, 2016) (excluding an expert opinion as to whether a drug met a certain standard pursuant to FDA regulations, as such "would require a legal interpretation" of that standard).

This Court has already held that Dr. Najafi's opinion that valsartan API is not bioequivalent to name brand valsartan is inadmissible because it "wades too far into the factfinder's domain." (*See* Ops. on Certification of Proposed Classes under FRCP Rule 23 and on Class Certification Expert Reports under FRE 702 ("Class Certification Ruling") at 91, ECF No. 2261.) Dr. Najafi now seeks to offer a host of similarly inappropriate opinions regarding defendants' purported non-compliance with FDA guidance and standards, including cGMP, and other applicable regulatory requirements. (*See, e.g.*, 10/31/22 Najafi Rep. at 38.) In addition, Dr. Najafi seeks to offer the legal conclusion that "[t]he Valsartan containing products that had NDMA and NDEA were adulterated (21 USC Section 351) [because] they were not manufactured in accordance with current good manufacturing practices" and "were not the same as the approved formulation and impurity profiles of [the Reference Listed Drugs] Diovan or Exforge because they contained NDMA and NDEA."

(10/31/22 Najafi Rep. at 38-39.) These opinions are precisely the type of legal/regulatory opinions that are barred under Third Circuit law, *Berckeley Inv. Grp., Ltd. v. Colkitt*, 455 F.3d 195, 217 (3d Cir. 2006); *Stanley*, 2014 WL 12573393, at *4, and they should be excluded here as well.

IV. DR. NAJAFI IS NOT QUALIFIED TO OPINE ON THE TOXICITY OF NDEA/NDMA OR GENERAL CAUSATION.

Finally, Dr. Najafi should be barred from offering opinions regarding the toxicity or carcinogenicity of valsartan API with NDMA or NDEA impurities (*see generally* 10/31/22 Najafi Rep.) because he is not a doctor, epidemiologist or toxicologist, *see, e.g.*, *Steele v. Aramark Corp.*, No. 09-4340 (JBS/JS), 2012 WL 1067879, at *19 (D.N.J. Mar. 29, 2012) (excluding physician's causation opinion as to whether toluene exposure caused kidney disease because of his "lack of specialization in . . . toxicology"), *on reconsideration in part*, 2012 WL 4103875 (D.N.J. Sept. 17, 2012), *rev'd in part on other grounds*, 535 F. App'x 137 (3d Cir. 2013); *Godreau-Rivera v. Coloplast Corp.*, 598 F. Supp. 3d 196, 215 (D. Del. 2022) ("since [expert] is not a toxicologist, he is not qualified to offer opinions on the toxicity of materials"); *Cunningham v. Masterwear, Inc.*, No. 1:04-cv-1616-JDT-WTL, 2007 WL 1164832, at *10 (S.D. Ind. Apr. 19, 2007) (excluding two experts from testifying to toxicology and causation where neither had "professional experience or training in toxicology or epidemiology"); *Blanchard v. Eli Lilly & Co.*, 207 F. Supp. 2d 308, 313 (D. Vt. 2002) (excluding expert psychiatrist's causation

opinion as to whether drug caused suicide where he "claim[ed] no expertise in . . . epidemiology . . . or toxicology"); *Sutera v. Perrier Grp. of Am. Inc.*, 986 F. Supp. 655, 667 (D. Mass. 1997) (excluding physician's opinion who "has no expertise in . . . toxicology" from determining the genesis of plaintiff's disease). Courts have also made clear that expertise in chemistry does not equate to expertise in toxicology. *See, e.g.*, *Cooper v. Lab'y Corp. of Am. Holdings*, 150 F.3d 376, 380 (4th Cir. 1998) (affirming the district court's exclusion of expert's testimony "because he was not a toxicologist and had no experience, beyond a general knowledge of chemistry, of forensic toxicology"). Accordingly, Dr. Najafi should not be allowed to testify about the alleged risks of NDMA or NDEA.

CONCLUSION

For the foregoing reasons, Dr. Najafi and Dr. Hecht's opinions should be excluded as outlined above.

Dated: March 13, 2023

Respectfully submitted,

By: */s/ Jessica Davidson*
Jessica Davidson (DC Bar No. 457021)
(Admitted to Practice in Maryland and the District of Columbia; Not Admitted in New York)
Liaison Counsel for Manufacturer Defendants
Allison M. Brown
SKADDEN, ARPS, SLATE, MEAGHER &

FLOM LLP
One Manhattan West
New York, NY 10001
Telephone: (212) 735-2588
Facsimile: (917) 777-2588
jessica.davidson@skadden.com
allison.brown@skadden.com

SKADDEN, ARPS, SLATE, MEAGHER & FLOM LLP
Nina R. Rose
1440 New York Ave., N.W.
Washington, D.C. 20005
Tel.: (202) 371-7000
Fax: (202) 661-0525
nina.rose@skadden.com

Attorneys for Zhejiang Huahai Pharmaceutical Co., Ltd., Huahai U.S., Inc., Prinston Pharmaceutical Inc., and Solco Healthcare U.S., LLC

Lori G. Cohen, Esq.
GREENBERG TRAURIG, LLP
Victoria Davis Lockard
Steven M. Harkins
Terminus 200
3333 Piedmont Rd., NE,
Suite 2500
Atlanta, Georgia 30305
Tel: (678) 553-2385
Fax: (678) 553-2386
cohenl@gtlaw.com
lockardv@gtlaw.com
harkinss@gtlaw.com

Gregory E. Ostfeld
Tiffany M. Andras
77 West Wacker Drive, Suite 3100
Chicago, Illinois 60601

Tel: (312) 456-8400
ostfeldg@gtlaw.com
andrast@gtlaw.com

Brian H. Rubenstein
1717 Arch Street, Suite 400
Philadelphia, Pennsylvania
Tel: (215) 988-7864
Fax: (214) 689-4419
rubensteinb@gtlaw.com

Attorneys for Teva Pharmaceuticals USA, Inc., Teva Pharmaceutical Industries Ltd., Actavis Pharma, Inc., and Actavis LLC

By: */s/ Alexia R. Brancato*
KIRKLAND & ELLIS LLP
Jay P. Lefkowitz
Devora W. Allon
Alexia R. Brancato
Brittney Nagle
601 Lexington Avenue
New York, New York 10022
Tel: (212) 446-5967
Fax: (212) 446-6460
lefkowitz@kirkland.com
devora.allon@kirkland.com
alexia.brancato@kirkland.com
brittney.nagle@kirkland.com

Attorneys for Torrent Pharmaceuticals Ltd. and Torrent Pharma Inc.

CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on March 13, 2023, I electronically filed the foregoing with the Clerk of the Court by using the CM/ECF system, which will send a notice of electronic filing to all CM/ECF participants in this matter.

/s/ *Jessica Davidson*
Jessica Davidson (DC Bar No. 457021)
(Admitted to Practice in Maryland and the District of Columbia; Not Admitted in New York)